

Analgesic effect of acupuncture needle penetration: a double-blind crossover study

NOBUARI TAKAKURA, HIROYOSHI YAJIMA

ABSTRACT

Background: Double-blind evaluation of acupuncture treatment has not previously been reported. We investigated the possible advantage of analgesic effects of needle penetration compared with skin pressure using non-penetrating needles in a double-blind study.

Methods: We conducted a double-blind crossover study of penetrating and non-penetrating (placebo) acupuncture trials. We recruited 56 healthy volunteers. They received painful electrical stimulation in the forearm for 1 minute before and immediately after and 10 minutes after each needle insertion to the LI-4 point, as well as 1 minute before, immediately after, and 10, 20, 30 and 40 minutes after the removal of the needle, which had remained in place for 20 minutes. After each application of electrical stimulation, the subjects rated the pain intensity using a numeric rating scale (0–150) comparing it with the baseline pain intensity (100) before the needle was applied. Pain from skin penetration and deep, dull pain (*de qi*) associated with needle application, which is considered essential for achieving successful acupuncture analgesia, were also recorded.

Results: We found no significant difference in analgesic effects between the penetrating and non-penetrating needle trials. In addition, no significant correlation was found between analgesic effect and *de qi*. A significant analgesic effect was observed during needle application and immediately after needle removal for both the penetrating and non-penetrating needle trials when compared with the no-acupuncture control condition (penetrating v. control: immediately, 10 minutes and 20 minutes after needle insertion [$p < 0.001$ for each] and immediately, 10 minutes and 20 minutes after needle removal [$p < 0.050$] for each; non-penetrating v. control: immediately, 10 minutes and 20 minutes after needle insertion [$p < 0.001$ for each] and immediately after needle removal [$p = 0.010$]).

Interpretation: Needle penetration did not confer a specific analgesic advantage over non-penetrating (placebo) needle application.

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Competing interests: Nobuaki Takakura and Hanada College possess a US patent (no. 6575992B1), a Canadian patent (no. CA 2339223), a Korean patent (no. 0478177), a Taiwan patent (no. 150135), a Chinese patent (no. ZL00800894.9) and a Japanese patent (no. 4061397) on the needles described in this article.

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ACUPUNCTURE HAS BEEN INCREASINGLY ACCEPTED as an alternative medical therapy for pain management. However, its efficacy has been controversial. The strongest evidence has come from single-blind trials in which patients were masked but practitioners were not.^{1,2} Some single-blind trials used placebo or sham needles,³⁻⁶ but they failed to meet the methodologic standards for blinding in current medical research.⁷⁻¹⁰ The reason for this is that it cannot be excluded that participants may be biased toward unblinded practitioners.⁷⁻¹⁵

Previously, no procedures or placebo needles were available to allow for a double-blind trial design.^{9,10,15} We recently developed a non-penetrating placebo needle that can be used to blind both acupuncturist and patient.^{16,17} With this placebo needle, we conducted a double-blind study of the analgesic effect of acupuncture. The aim was to determine whether the single, simple needle had specific analgesic effects over the non-penetrating placebo needle¹⁶⁻¹⁹ under double-blind conditions.

Methods

Study design. We conducted a double-blind crossover study that compared the analgesic effects of penetrating and non-penetrating (placebo) needle trials in healthy volunteers. The study was conducted in the Japan School of Acupuncture, Moxibustion and Physiotherapy, the educational foundation Hanada Gakuen, Tokyo, Japan.

Because of resource constraints, we used a crossover design, which was developed to maintain most factors as constants.²⁰ The statistical significance of these crossover designs was further improved by eliminating most interpatient variances, as compared with the parallel-group designs that include more patients.²⁰

The study was approved by the Ethics Committee of Showa University.

Participants. We recruited 56 eligible healthy volunteers (31 men, 25 women) from the Japan School of Acupuncture, Moxibustion and Physiotherapy who were familiar with acupuncture treatment. Their mean age was 32.1 (standard deviation 9.9) years (Table 1). Sub-

jects with any signs of a neurological disorder, those using painkillers or psychotropic drugs, and those with dermatological disease were excluded. Before recruitment the subjects were already aware that acupuncture needles are categorized traditionally into 2 types — penetrating and non-penetrating — and that either type may be used in acupuncture treatments. The purpose and format of the study were explained, and written informed consent was obtained from the subjects before the study.

Two experienced licensed acupuncturists participated in the study. To limit bias, one of the acupuncturists applied all of the needles, and the other removed them.

Assignment. Each of the 56 sterilized penetrating needles (insertion depth of 10 mm²¹) and 56 non-penetrating needles was sealed in a small, sterilized opaque container. We prepared 56 opaque envelopes, one per subject, that contained a pair of containers. Neither the practitioner nor the subjects knew which container housed which needle in the envelope.

Immediately before the first needle trial, the acupuncturist blindly selected a container from the envelope and used the needle in it for the first acupuncture application. In the second needle application, the acupuncturist used the needle from the other container. To prevent any carry-over analgesic effect, the 2 trials were conducted more than 24 hours apart.^{22,23}

Intervention blinding. The experimental pain-eliciting procedure was explained to the subjects when they were informed about the study protocol and needle trials. To maximize the effectiveness of masking and minimize the bias, the subjects were not informed about the possible use of non-penetrating needles throughout the study.⁷

For the placebo needles, we used non-penetrating needles with a blunt tip that pressed against the skin but did not penetrate it. To practitioners, they were designed to match the appearance and feel of the penetrating needles when inserted to a specified depth (Fig. 1), as described previously.^{16,17} To patients the appearance and feel of the non-penetrating needles were found to be indistinguishable from the penetrating needles, and some of the penetrating needles were indistinguishable from the non-penetrating needles (Fig. 1).^{16,17,24}

Table 1: Age and sex of the 56 study subjects, by type of acupuncture needle received first

Characteristic	All subjects (n = 56)	Penetrating needle first (n = 21)	Non-penetrating (placebo) needle first (n = 35)
Age, yr, mean (SD)	32.1 (9.9)	30.9 (10.3)	32.9 (9.7)
Male sex, %	55.4	71.4	45.7
SD = standard deviation			

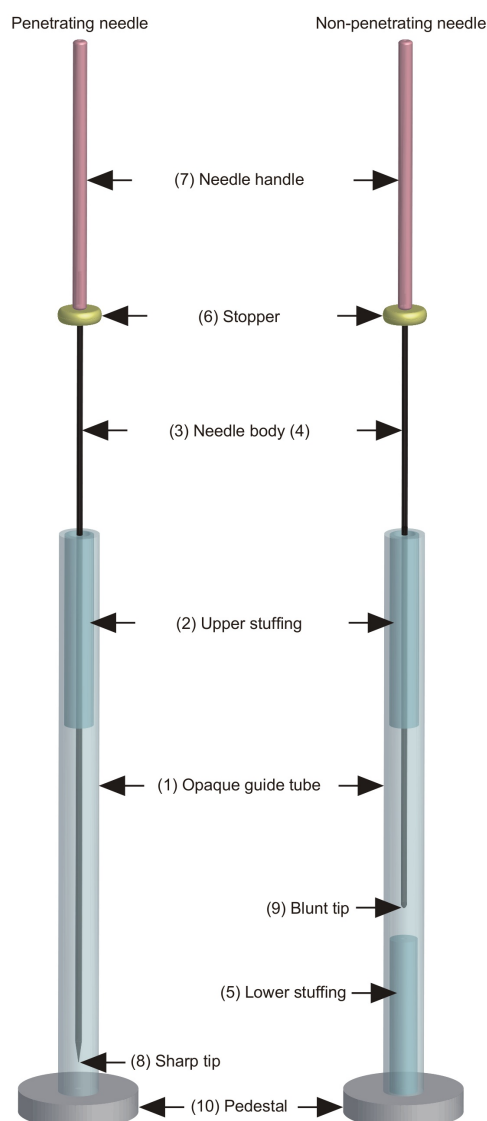


Figure 1. Penetrating and non-penetrating (placebo) needles. Each needle assembly comprises an opaque guide tube (1) and upper stuffing (2) to provide resistance to the needle body during its passage through the guide tube. The body of the penetrating needle (3) is longer than the guide tube by an amount equal to the insertion depth. The body of the non-penetrating needle (4) is long enough to allow its blunt tip to press against the skin when the needle body is advanced to its limit. The non-penetrating needle contains stuffing in the lower section (5) to give a sensation similar to that of skin puncture and tissue penetration. Both needles have a stopper (6) that prevents the needle handle (7) from advancing further when the sharp tip of the penetrating needle (8) or the blunt tip of the non-penetrating needle (9) reaches the specified position. The pedestal (10) on each needle is adhesive, allowing it to adhere firmly to the skin surface. The diameter of the needles used in this study was 0.16 mm.

Before the study began, the acupuncturist who applied all of the needles was informed about the use of both non-penetrating and penetrating needles during the trials. After insertion of each needle, he was asked to record whether he thought the needle was “penetrating,” “non-penetrating” or “unidentifiable.” A goodness-of-fit χ^2 test was used to determine that the number of correctly and incorrectly identified needles fitted a probability of 0.5.^{16,17,24}

We took every precaution to ensure that identical experimental conditions were maintained from the first to the last subject. Not only the acupuncturists and assistant but also the needles were the same. Needle quality was maintained throughout the study. Throughout the trial, the subjects were blindfolded except when they were asked to measure pain intensity from the electrical stimulation or to measure the pain from skin penetration and the *de qi* (deep pain) associated with needle application. Each needle trial was performed at about the same time on different days.

Needle application. For each needle trial, the acupuncturist applied the needle to the subject’s right hand at the LI-4 point (the large-intestine meridian — the most important analgesic point.^{21–23} He used the alternating twirling technique (alternating between rotating the needle clockwise and counterclockwise).^{16,17,24}

The needle was left in place for 20 minutes.²³ After 20 minutes, the needle body was returned to its initial position in an opaque guide tube. The entire needle assembly was removed from the skin and sealed in an opaque envelope by the second acupuncturist, who re-confirmed the accuracy of the needle location at the LI-4 point.

We took all possible precautions to ensure that the identity of the needle was not revealed to the practitioner, the subjects or the investigators during the acupuncture trials.

Pain-eliciting electrical stimulation. Subjects reclined on a bed in the supine position with their right hand resting by the side of their body. A trained assistant with little knowledge of acupuncture delivered painful electrical stimulation to the middle of the posterior surface of the right forearm through surface electrodes using a constant-voltage isolation unit (SEN-3301, SS-104 J; Nihon Kohden Corp., Tokyo, Japan).^{22,23,25–27} The strength of the stimulation (square wave pulse: duration 1 ms; interval 1 s) that produced a clear sensation of pain (voltage, pain threshold \times 1.1–1.2) in each subject was determined before each trial of the no-acupuncture control, penetrating-needle and non-penetrating needle conditions. The mean intensities for each of the three conditions did not differ significantly from each other (no-acupuncture control 69.2 ± 20.4 V; penetrating needle trial 69.9 ± 22.0 V; and non-

penetrating needle trial 70.0 ± 22.8 V) (Wilcoxon test, $p = 0.94$). Pain thresholds remained stable over time for individual subjects.

Five minutes before each needle insertion, the trained assistant delivered the electrical stimulation for 1 minute to provide a baseline reading for pain. The assistant then delivered the electrical stimulation (square wave pulse: duration 1 ms; interval 5 s for 1 minute immediately after and 10 minutes after each needle insertion as well as 1 minute before, immediately after and 10, 20, 30 and 40 minutes after the removal of the needle.

Outcome measures. The primary outcome measure was pain elicited when electrical stimulation was applied to the posterior forearm. To test the reliability of pain measurement before the needle trials, we asked the subjects to measure the pain intensity without application of the needles (no-acupuncture control condition). We used the same methods and time intervals for this control condition as those in the needle trials.

Immediately after each episode of painful stimulation, subjects were shown a numeric rate scale ranging from 0 (no pain) to 150; the scale was based on one from a previous placebo study.²⁸ The subjects were asked to rate the pain intensity and compare it with the baseline pain intensity (arbitrarily assigned a score of 100) before each needle application.

The secondary outcome measures were the pain from skin penetration and the *de qi* (deep dull pain) as-

sociated with needle application. Subjects rated the pain from skin penetration and the *de qi* using a visual analogue scale ranging from 0 (no pain or *de qi*) to 10 (the most intense pain or *de qi*).^{3,17,24}

Subjects were also asked to report anything that they noticed, however trivial, regarding the needle application.¹⁶

Adverse events. We monitored the subjects for the presence of adverse events such as pneumothorax, bleeding, hematoma, dizziness, tiredness and needle pain. We also asked the subjects to report if they experienced any adverse event after acupuncture treatment.

Statistical analysis. We compared the pain intensity scores for the three conditions (penetrating needle, non-penetrating needle and no-acupuncture control) using the Wilcoxon signed-ranks test to identify pairwise group differences. To determine whether there was an order or carry-over effect, we compared the pain intensity scores between the group given the penetrating needle first ($n = 35$) and the group given the non-penetrating needle first ($n = 21$) for the penetrating and non-penetrating needles, respectively, using the Wilcoxon signed-ranks test.

We used the Wilcoxon signed-ranks test to compare all possible combinations of non-penetrating needle trial and skin-penetration pain ($n = 34$); non-penetrating needle trial and no skin-penetration pain ($n = 22$); penetrating needle trial and skin-penetration pain ($n = 44$); and penetrating needle trial and no skin-penetration pain ($n = 12$). We also used the Wilcoxon signed-ranks test to compare all possible combinations of non-penetrating needle trial and *de qi* ($n = 23$); non-penetrating needle trial and no *de qi* ($n = 33$); penetrating needle trial and *de qi* ($n = 33$); and penetrating needle trial and no *de qi* ($n = 23$). The identity of the test needles was revealed only after tabulating the results.

Statistical comparisons between the penetrating needle and non-penetrating needle conditions in relation to the visual analogue scale scores for skin-penetration pain and *de qi* were made using the Wilcoxon signed-ranks test. Spearman's rank correlation coefficient was used to indicate the relation between pain intensity and *de qi*.

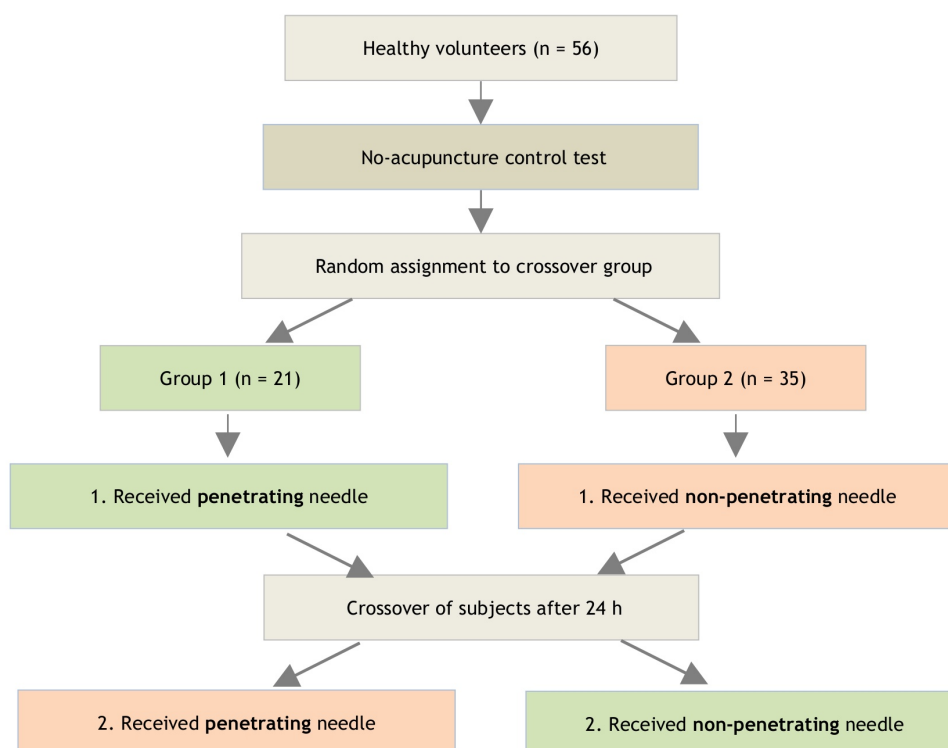


Figure 2. Flow of subjects through the study protocol

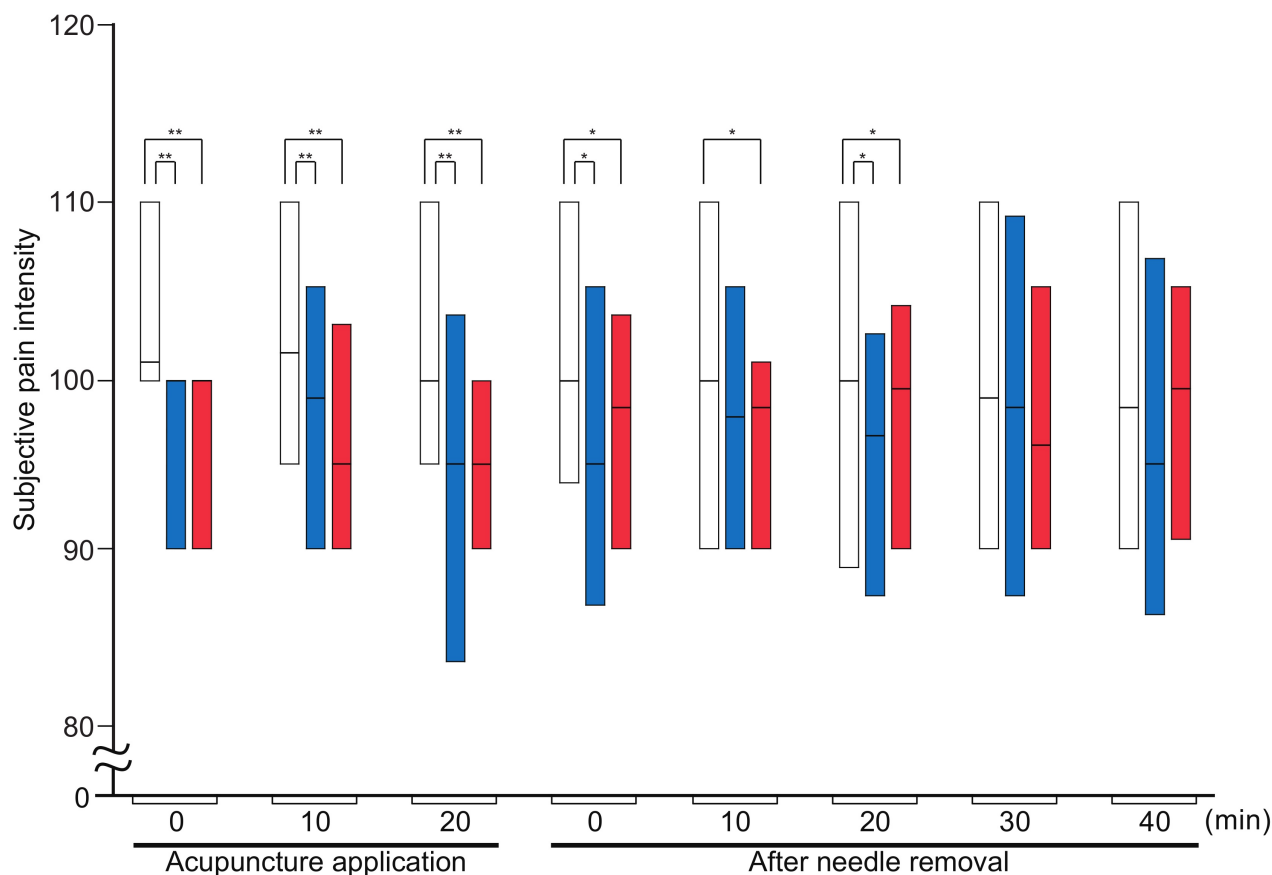


Figure 3. Changes in pain intensity rated by the 56 subjects during and after application of the penetrating (red) and non-penetrating (blue) needles and during the no-acupuncture control condition (white). The top, middle and bottom lines of the boxes correspond to the 75th, 50th (median) and 25th percentiles, respectively. The whiskers extend from the 10th to the 90th percentile. The filled circles indicate the arithmetic mean. * $p < 0.05$, ** $p < 0.01$. (Note: At zero minutes after the acupuncture application, the medians and 75th percentiles were 100 for both needle groups.)

Results

The study started in July 2000 and was completed in July 2005. The flow of the subjects during the study is shown in Fig. 2. All 56 subjects completed the study. Twenty-one subjects received the penetrating needle first, and 35 received the non-penetrating (placebo) needle first. Both the groups fitted a probability of 0.5 ($\chi^2 = 3.5$, $p = 0.06$).

Pain intensity. We found no significant difference between the analgesic effects of the penetrating and non-penetrating needles when measured at all the time points (Fig. 3). In addition, we found no significant differences in pain intensity between the group who received the penetrating needle first and the group who received the non-penetrating needle first

for either the penetrating needle ($p = 0.22$) or the non-penetrating needle ($p = 0.15$), respectively. No carry-over or order effect was observed.

When compared with the no-acupuncture control condition, both the penetrating and non-penetrating needle trials resulted in a significant analgesic effect (penetrating v. control: immediately, 10 minutes and 20 minutes after needle insertion [$p < 0.001$ for each]; non-penetrating v. control: immediately, 10 minutes and 20 minutes after needle insertion [$p < 0.001$ for each]). The analgesic effect lasted until 20 minutes after removal of the penetrating needle (penetrating v. control: immediately [$p = 0.015$], 10 minutes [$p = 0.021$] and 20 minutes [$p = 0.033$] after needle removal). It lasted until immediately after the removal of the non-penetrating needle (non-penetrating v. control: immediately after [$p < 0.01$]) (Fig. 3).

Pain from skin penetration and *de qi*.

The pain from skin penetration and *de qi* (deep dull pain) upon application of the penetrating needle (median [mean \pm sd]: skin penetration, 2 [3.3 \pm 3.2], *de qi*, 2 [2.8 \pm 3.1]) was significantly greater than that experienced upon application of the non-penetrating needle (skin penetration, 1 [1.6 \pm 2.2], *de qi*, 0 [1.1 \pm 1.8]) ($p < 0.01$). The pain intensity among the subjects who perceived needle sensations was not significantly less than the pain intensity among those who did not perceive needle sensations for both types of needles at all of the time points measured (Fig. 4).

At all measurement points, we found no significant correlation between pain intensity and skin-penetration pain, or between pain intensity and *de qi* for the penetrating and non-penetrating needles.

Effect of blinding. The acupuncturist identified 33 needles correctly and 31 incorrectly; he recorded 48 needles as “unidentifiable.” The 33 correct and 31 incorrect identifications fit a probability of 0.5 ($\chi^2 = 0.06$, $p = 0.80$), after exclusion of the 48 unidentifiable needles. None of the subjects commented that they had received a non-penetrating needle. As in a previous study,^{16,17} about 20% of the penetrating needles elicited neither skin-penetration pain nor *de qi*. Although small in proportion, this finding suggested that penetrating needles have some potential for double masking.

Adverse events. No serious or minor adverse events were observed during the experiment or reported by the subjects after the trial.

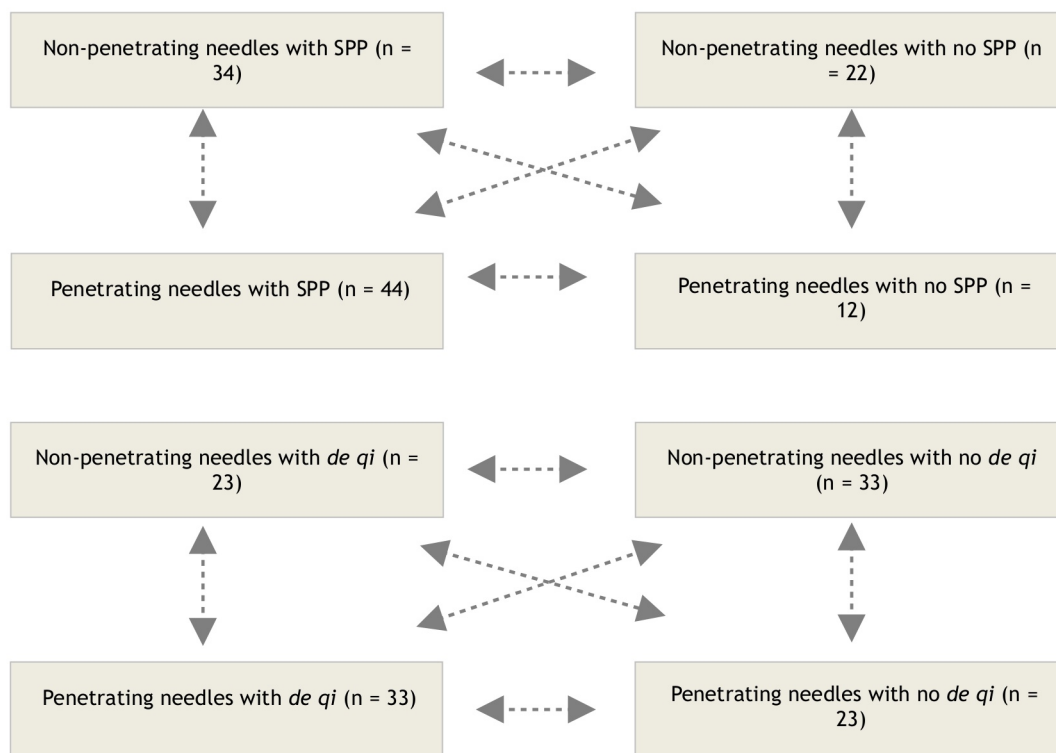


Figure 4. Relation between needle sensation and analgesic effect of acupuncture.

Comparison of pain intensity scores between subjects who felt needle sensation (skin pain from penetration [SPP] or from *de qi*, deep dull pain associated with acupuncture treatment) with the non-penetrating needle; subjects who felt no needle sensation with the non-penetrating needle; subjects who felt needle sensation with the penetrating needle; and subjects who felt no needle sensation with the penetrating needle.

Throughout the study, there was no significant difference ($p > 0.05$) between the pairs of groups designated by broken arrows.

Interpretation

In this double-blind study, we found that the analgesic effect from the skin penetration and deep needle insertion (a distinctive feature of acupuncture) with the penetrating needle was no greater than the analgesic effect from the skin pressure alone with the non-penetrating needle. The analgesic effect produced by the penetrating needle was relatively weak and less persistent compared with previous studies that were performed without effective double-blind controls.^{22,23} Furthermore, we found no significant correlation between the analgesic effect and *de qi*, which has been considered essential for acupuncture analgesia.²¹

Our study has several limitations. First, the analgesia produced by skin pressure with the non-penetrating needles, which may stimulate high-threshold skin mechanoreceptors,²⁹ may mimic the analgesic effect ex-

perienced in acupressure treatments.³⁰ Further research using appropriate controls is required for addressing this issue.

Second, in practice, additional manipulations or adjustments to the insertion depth and direction of the needle are performed after penetration to achieve *de qi* with each needle application.^{1,2} In our study, the needles were designed to provide uniform direction and depth of needle insertion in all subjects. In addition, we did not conduct additional manipulation after needle insertion. Therefore, all of the subjects received the same stimulus to allow comparison of the effects of needle application. We believe a change in stimulus would likely have changed our outcomes of interest. However, the pain intensity among subjects who perceived *de qi* with penetrating and non-penetrating needles was not less than the pain intensity among those who did not perceive *de qi*. As such, it is possible that *de qi* is not a precondition of subsequent acupuncture analgesia.

Third, we selected a crossover design because of resource constraints. As reported previously, crossover designs have often shown greater statistical power than parallel-group designs with large samples.²⁰ In our case, although our sample was relatively small, it was sufficient to apply the Wilcoxon signed-ranks test to reveal a significant difference in analgesic effect between the penetrating and non-penetrating needles. Although the small sample was a potential limitation, the differences obtained between the two types of needles would be sufficiently small to be considered clinically significant.³¹

Fourth, there may have been a carry-over analgesic effect of the treatment. To prevent a carry-over effect, we designed the study so that there would be an interval of at least 24 hours between the two needle trials. This interval was determined based on findings from previous studies, where alleviation of experimental pain with acupuncture at the LI-4 point was maintained for about 1 hour after needle removal with manual acupuncture²³ and for up to 16 hours after needle removal with electrical acupuncture.²² In our study, significant alleviation of pain was observed only until 20 minutes after needle removal. We observed no significant difference in pain intensity between the group who received the penetrating needle first and the group who received the non-penetrating needle first; therefore, we believe the results were not biased by the carry-over or order effect.

We believe that our method of blinding practitioners using validated double-blind needles^{16,17,24} was successful and that the subjects were unaware of the use of non-penetrating blunt-tipped needles as in previous studies.^{3-6,16-19} However, the successful blinding of subjects should be interpreted with caution: the subjects were not specifically asked whether they believed they had received a penetrating or a non-penetrating needle.

Despite these limitations, our results support the use of double-blind methodology in future acupuncture research. Large randomized controlled double-blind trials

involving different types of pain (e.g., secondary pain after excessive tonic muscle tension) in which patients are informed of the possible use of non-penetrating needles are necessary. Also, further studies are required to determine the relation between analgesia and *de qi* elicited after needle insertion.

Contributors: Nobuari Takakura designed the double-blind needles and the study, collected the data, performed the analysis and wrote the manuscript. Hiroyoshi Yajima contributed to the study design, the collection and analysis of data, and the preparation of the manuscript. Both authors approved the final version submitted for publication. Nobuari Takakura is the guarantor.

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